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EXAMINER	
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1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,028	BRAHMBHATT ET AL.	
	Examiner	Art Unit	
	ANOOP SINGH	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-7,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-27 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/5/09, 12/2/08, 8/1/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the papers filed December 15, 2008. Applicant's response to restriction requirement to the claims filed December 15, 2008, has been entered. Currently, claims 1-30 are pending.

Election/Restrictions

Applicants' election of claims 8-33 and 38 (Group II) directed to drug delivery method in the reply filed on January 15, 2009 is acknowledged. It is noted that restriction requirement mailed dated 10/16/2008 required election of a prior version of claims and not the claims that were amended and entered during international phase of PCT/IB2005/000204 filed August 1, 2006. As correctly indicated by applicants that pending claims are similar to prior claims, therefore pending claims have been grouped in the same manner as indicated in previous office action dated 10/16/2008 and also suggested by applicants in response to office action. Examiner confirms that this application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1 for the reasons of record. The new groups are: group I, claims 1-7, 29 (drawn to a composition comprising intact minicells that contain a drug), group II (claims 8-27 and 30, drawn to a drug delivery method) and group III (claim 28, drawn to a method of loading minicells). During a telephone conversation with Mr. Brian McCaslin on 3/10/2009, an election without traverse was confirmed for claims 8-27 and 30 (group II). Applicants have also elected polypeptide as species for bispecific ligand. Upon further consideration election of species requirement is withdrawn and all the species of bispecific ligand is rejoined for the examination purpose. Claims 1-7, 28-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on

January 15, 2008. As the restriction is deemed proper, the requirement for restriction is hereby made FINAL.

Claims 8-27 and 30 drawn to a drug delivery method are under examination.

Information Disclosure Statement

Applicants' IDS, filed 01/05/2009, 12/02/2008 and 08/01/2006 have been considered.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. In the instant case, applicants have cited multiple references in the specification but they have not been considered by the Examiner as no copy of any of the publication was provided.

Claim Objections

Claim 30 is objected to because of the following informalities: an independent claim must start with an article "a" and, therefore, claim 30 should recite "A method of using..". Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

> section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8-12, 15-19, 21-24, 26-27 and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Sabbadini et al. (US 7,183,105, dated 2/27/2007, filed 5/28/2002, effective filing date 2/25/2002).

Claims are directed to a targeted drug delivery method that comprises bringing bispecific ligands into contact with (a) bacterially derived minicells that contain a drug molecule and (b) target mammalian cells, such that (i) said bispecific ligands cause said minicells to bind to said mammalian cells, (ii) said minicells are engulfed by said mammalian cells, and (iii) said drug is released into the cytoplasm of said mammalian cells. Subsequent claims limit the method of 1 wherein said target mammalian cells are non phagocytic cell and bispecific ligand comprises polypeptide or carbohydrate and wherein said bispecific ligand comprises a first arm that carries specificity for a bacterially derived minicell surface structure and a second arm that carries specificity for a non-phagocytic mammalian cell surface receptor. Claim 17 limits the bispecific ligand of claim 1 to include an antibody or antibody fragment. Claim 19 limits the minicells of claim 1 to an intact cell wall. Claims 21-22 limit the method wherein mammalian cells are under *in vitro* or *in vivo* condition. Claims 23-24, 26-27 are directed to a drug delivery method comprising brining minicell containing small molecule drug into contact with a cell that are endocytosis such that minicell are engulfed and the drug is released in the cytoplasm of the cells.

Claim 30 is included in the rejection because of the breadth of the claims. The rejection is applied to the extent method only requires administering minicells containing small molecule drug and a bispecific ligand that is capable of binding minicells and target non phagocytic mammalian cell to a cell, tissue or organ. The rejection is not to a method of treating a disease or modifying trait. The bispecific ligand comprising first arm that carries specificity for minicells surface and a

second arm that carries specificity for cell surface receptor has been interpreted as being equivalent to the attachment of an antibody that binds to a ligand specific to a minicell as well as receptor on to the mammalian cell surface, as first and second arm respectively.

With respect to claims 8-12 and 23, Sabbadini et al. teach a targeted drug delivery method comprising contacting a target mammalian cell with a minicell coated with an antibody as a binding moiety capable of binding to a ligand present on the surface of the target mammalian cell, wherein the minicell comprises the small molecule, and wherein the contents of the minicell are delivered into the cell from a minicell bound to the cell (col. 17, 6-15, col. 7, lines 10-15, col. 136, lines 58-66). Sabbadini et al. also teach that the minicells of the invention are capable of encapsulating and/or loading into a membrane a variety of substances that includes small molecules (see column 161, lines 37-46, column 17, line 16). Sabbadini et al teach that the minicells are engulfed by cells by a process such as receptor mediated endocytosis (see col. 171, line 55). Additionally, it is also disclosed that the method results in transfer of the molecule from the interior of a minicell into the cytoplasm of the target cell (see col. 24, line 22, col. 165, lines 5-10). Sabbadini et al disclose that the target mammalian cell may include cos and A-431 cancer cell line that are non phagocytic mammalian cell (column 252, line 30 and 55, limitation of claim 9). It is also disclosed that the cell displays a ligand specifically recognized by a binding moiety attached to the minicell. The moiety to be conjugated to the minicells can be a polypeptide (limitation of claim10). It is also disclosed that an antibody can be covalently attached as a binding moiety (see column 136, lines 58-66), which binds to ligand present on the surface of a mammalian cell. Thus, bispecific ligand comprises a covalent attachment of an antibody that binds to a ligand specific of a minicell outer membrane protein as well as receptor on to the mammalian cell surface, as first and second arm respectively (limitation of claims 11 and 15). Sabbadini et al also teach minicell comprising a therapeutic agent displays a

binding moiety such as antibody that specifically binds a receptor present on the surface of a non phagocytic cell meeting the limitation of first and second arm being monospecific (col. 7, lines 6-15, limitation of claim 12). Regarding claim 16, Sabbadini et al disclose mammalian cell surface display receptor such as EGFR that is capable of activating receptor mediated endocytosis with minicell (see example 19). Sabbadini et al teach that the antibody may be a single chain antibody (see col. 132, line 60) or a humanized antibody (col. 132, line 53) (limitation of claims 17 -18). Sabbadini et al also teach contacting target tumor cells with minicells containing toxic drug molecule coated with an antibody that is capable of binding a ligand on the surface of the tumor cell, wherein minicells are engulfed by the tumor cell by receptor mediated endocytosis, thereby releasing toxic drug into the tumor cell (see column 171, col. 1, line 62-65, limitation of claims 23). With respect to claims 19 and 24, Sabbadini et al disclose that the minicells produced contains an intact cell wall (see col. 39, lines 34-35, and claims 1, 8 in '105). With respect to claims 21-22, 26-27, Sabbadini et al. teach that method of targeted drug delivery using minicell can be carried out under *in vitro* or *in vivo* condition (see col. column 11, line 14 and col. 36, lines 56-59).With respect to claim 30, Sabbadini et al disclose a method of directly injecting intact minicell coated with antibody capable of binding minicells to the target tumor cell, wherein minicell contain toxic substance, minicell coated with antitumor antibodies target a tumor cell and deliver cytotoxic substance to the tumor (column 171, lines 62-65 to col. 172, lines 1-3). It is noted that using this approach Sabbadini et al contemplated delivering therapeutic drug to test the efficacy of drug delivery in A-431 cancer cell line (human epithelial carcinoma cell line) (see column 252, line 30 and 55) meeting the limitation of claim 30. Accordingly, Sabbadini et al. anticipates claims 8-12, 15-19, 21-24, 26-27 and 30.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8, 11, 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sabbadini et al. (US 7,183,105, dated 2/27/2007, filed 5/28/2002, effective filing date 2/25/2002), Nettelbeck et al (Mol Ther. 2001; 3(6):882-91, IDS) and Coldwell et al (The Journal of Immunology, 1984, 133, 2 950-957).

With respect to claims 8, 11, Sabbadini et al. teach a targeted drug delivery method comprising contacting a mammalian cell with minicell coated with an antibody as a binding moiety capable of binding to a ligand present on the surface of said mammalian cell, wherein the minicell comprises the small molecule, and wherein the contents of the minicell are delivered into the cell from a minicell bound to the cell (col. 17, 6-15, col. 7, lines 10-15, col. 136, lines 58-66). Sabbadini et al. also teach that the minicells of the invention are capable of encapsulating and/or loading into a membrane a variety of substances that includes small molecules (see column 161, lines 37-46, column 17, line 16). Sabbadini et al teach that the

minicells are engulfed by cells by a process such as receptor mediated endocytosis (see col. 171, line 55). Additionally, the method disclosed by Sabbadini et al results in transfer of the molecule from the interior of a minicell into the cytoplasm of the target cell (see col. 24, line 22, col. 165, lines 5-10). Sabbadini et al disclose that the target mammalian cell may include cos and A-431 cancer cell line that are non phagocytic mammalian cell (column 252, line 30 and 55). It is also disclosed that an antibody can be covalently attached as a binding moiety (see column 136, lines 58-66), which binds to ligand present on the surface of a mammalian cell. Although, Sabbadini et al. teach a method of drug delivery by covalently attaching binding moieties such as antibody to minicells such that it binds to a ligand present on the surface of a mammalian cell, but differed form claimed invention by not explicitly disclosing that the first arm specific to an O-polysaccharide component of LPS or first and second arm are multivalent.

However, prior to instant invention, Nettelbeck et al teach a recombinant antibody as a molecular bridge, linking the virus capsid to the endothelial cell surface protein endoglin, for vascular targeting of adenoviruses (abstract). It is noted that Nettelbeck et al also disclose a method to construct bispecific single chain multivalent antibody directed against endoglin and the adenovirus knob domain (see 885, col.1, para.4). It is also disclosed that the ScFv C4 (endoglin) and the neutralizing anti-knob scFv S11 are combined in a bispecific single-chain diabody (scDb EDG-Ad) (see figure 3) for experimental analysis. Nettelbeck et al reported enhanced oviral infectivity mediated by scDb EDG-Ad that was restricted to endoglin-positive cells showing cell specific targeting (see figure 6, page 889, col. 2, para. 2).

Although Nettelbeck et al describes the advantage of using bispecific diabody to target viral fiber knob domain to endoglin expressing cancer cell, but differed from claimed invention by not disclosing first arm specific to an O-polysaccharide of a LPS.

Prior to instant invention, Coldwell et al teach production of monoclonal antibodies to antigenic determinants of the O-polysaccharide of *Salmonella typhimurium* lipopolysaccharide (LPS) (abstract).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the respective teachings of Sabbadini et al, Nettelbeck et al and Coldwell by using an antibody to bring together intact minicell and mammalian cell such that minicell binds to mammalian cell and minicell that are engulfed by the mammalian cell with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would have been motivated to use an single chain antibody diabody as a molecular bridge, linking the O-polysaccharide of the minicell to the endothelial cell surface protein endoglin (diabody) as a matter of design choice to obtain more specific delivery of therapeutic agent as described by Nettelbeck, said design choice amounting to combining prior art elements according to known methods to yield predictable results. One who would have practiced the invention would have had reasonable expectation of success since Sabbadini et al had already taught a method for targeted delivery of small moelcule by attaching an antibody to a bacterial minicells that specifically binds a ligand present on the surface of a mammalian cell, while combining the teaching of Sabbadini et al with those in Nettelbeck and Coldwell would have resulted in specific small molecule transfer into endoglin positive endothelial cell.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 8, 20, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sabbadini et al. (US 7,183,105, dated 2/27/2007, filed 5/28/2002, effective filing date 2/25/2002) and Hope et al (WO/1996/026715, dated 06/09/1996, IDS)

With respect to claims 8, 23, Sabbadini et al. teach a targeted drug delivery method comprising contacting a mammalian cell with minicell coated with an antibody as a binding moiety capable of binding to a ligand present on the surface of said mammalian cell, wherein the minicell comprises the small molecule, and wherein the contents of the minicell are delivered into the cell from a minicell bound to the cell (col. 17, 6-16, col. 7, lines 10-15, col. 136, lines 58-66). Sabbadini et al. also teach that the minicells of the invention are capable of encapsulating and/or loading into a membrane a variety of substances including small molecules and antibiotics (see column 161, lines 37-46). It is also disclosed that an antibody can be covalently attached as a binding moiety (see column 136, lines 58-66), which binds to ligand present on the surface of a mammalian cell. Sabbadini et al also teach that minicells are engulfed by the cell by receptor mediated endocytosis (see column 171, col. 1, line 62-65). Regarding claim 23, Sabbadini et al also teach contacting target tumor cells with minicells containing toxic drug molecule coated with an antibody that is capable of binding a ligand on the surface of the tumor cell, wherein minicells are engulfed by the tumor cell by phagocytosis or receptor mediated endocytosis, thereby releasing toxic drug into the tumor cell (see column 171, col. 1, line 62-65).

Although, Sabbadini et al. teach a method of drug delivery by covalently attaching an antibody to minicells capable of encapsulating into a membrane small molecules such that antibody at the surface of minicell binds to a ligand present on the surface of a mammalian cell, but differed form claimed invention by not teaching encapsulation of a chemotherapeutic agent.

However, prior to instant invention, it was routine in the art to package/load chemotherapeutic drugs such that diffusion across the phospholipid bilayer-membrane is unidirectional for targeted delivery of the molecule. For instance, Hope et al teach a method a method involves loading a chemotherapeutic agent such as doxorubicin into preformed lipid bilayer of liposome having a concentration

gradient across the lipid bilayer (see Figure 1). It is noted that Hope et al disclose that the structure of the lipid bilayer is similar to the membranes enveloping animal cells (see page 1, line 21).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the respective teachings of Sabbadini et al, Hope by modifying the method of targeted drug delivery of Sabbadini et al by loading chemotherapeutic agent such as doxorubicin into minicell using the method disclosed by Hope with a reasonable expectation of achieving predictable result. A person of skill in the art would have been motivated to encapsulate doxorubicin into the minicell because Sabbadini et al embraced the potential of delivering cytotoxic agent specifically to the tumor for cancer therapy (supra). One who would have practiced the invention would have had reasonable expectation of success since Hope had already taught a method for loading doxorubicin in a preformed lipid bilayer having a concentration gradient across the lipid bilayer, while Sabbadini et al disclosed that cellular membrane of the minicell is a lipid bilayer that forms the boundary between the interior of a cell and its external environment. Thus, it would have required routine experimentation for one of ordinary skill in the art to combine the teachings of Sabbadini et al with those of Hope to load doxorubicin or any other acidic or basic chemo therapeutic in the minicell for targeted drug delivery to enhance the therapeutic effect.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-9, 16, 19-27 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-44, 48-51 and 73 of copending Application No. 11/765635. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are directed to overlapping subject matter. Claims in the instant application are directed to a targeted drug delivery method that comprises bringing bispecific ligands into contact with (a) bacterially derived minicells that contain a drug molecule and (b) target mammalian cells, such that (i) said bispecific ligands cause said minicells to bind to said mammalian cells, (ii) said minicells are engulfed by said mammalian cells, and (iii) said drug is released into the cytoplasm of said mammalian cells. Subsequent claims limit the method of 1 wherein said target mammalian cells are non phagocytic cell. Claims further limit the method according to base claim 8, wherein mammalian cell surface receptor is capable of activating receptor-mediated endocytosis of said minicells. Claim 19 limits the minicells of claim 1 to an intact cell wall. Claim 20 limits the small molecule drug to include a chemotherapeutic agent. Claims 21-22 limit the method wherein

mammalian cells are under *in vitro* or *in vivo* condition. Claims 23-27 are directed to a drug delivery method comprising brining minicell containing small molecule drug into contact with a cell that are endocytosis such that minicell are engulfed and the drug is released in the cytoplasm of the cells. Claim 30 requires administering minicells containing small molecule drug and a bispecific ligand that is capable of binding minicells and target non phagocytic mammalian cell to a cell, tissue or organ. In contrast, claim in 40-44, 48-51 and 73 of copending Application No. 11/765635 is directed to targeted drug delivery method that comprises bringing bispecific ligands into contact with (a) killed bacterial cells that contain a drug molecule and (b) target mammalian cells, such that (i) said bispecific ligands cause said killed bacterial cells to bind to said mammalian cells, (ii) said killed bacterial cells are engulfed by said mammalian cells, and (iii) said drug is released into the cytoplasm of said mammalian cells. Claims 41 and 42 limit the method of claim 40 wherein said target mammalian cells are non-phagocytic cells and said drug is a chemotherapeutic agent. Claims 43-44 limit the method of claim 40 to include, wherein said mammalian cells are in vitro and in vivo respectively. It is noted that claims 48 is drawn to a drug delivery method that comprises bringing killed bacterial cells that contain a drug into contact with mammalian cells that are phagocytosis- or endocytosis-competent, such that said killed bacterial cells are engulfed by said mammalian cells and said drug is released into the cytoplasm of said mammalian cells. Claim 49 limits the method to include drug that is a chemotherapeutic agent, while mammalian cells are in vitro (claim 50) or in vivo(claim 51). Claims 73 is directed to use of bacterial cells and bispecific ligands in the preparation of a medicament, said bacterial cells containing a drug, and said bispecific ligands being capable of binding to said bacterial cells and to target non-phagocytic mammalian cells, for use in a method of treating a disease or modifying a trait by administration of said medicament to a cell, tissue, or organ. It is noted that claims in the instant application differ only with respect to a narrower scope of

bispecific ligand, which encompasses those specifically claimed in application '635. Each of the claim sets are directed to a method that involves intact bacterial cells with overlapping methods. The claims of application '635 and the instant claims are considered obvious in view of each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Tomlinson I et al (.Methods Enzymol, 2000, 326, 461-479) teach a method for generating multivalent and bispecific antibody fragments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anoop Singh/
Examiner, Art Unit 1632